REMARKS

Applicants would like to thank Examiner Jones for taking the time to discuss this case in a telephonic interview on October 3, 2006.

Applicants have amended Claims 1, 9-12, 26, 28, 38, 39, 49, 87, 88, and 93 herein for clarity. Enabling support for the amendments can be found in the application as filed, and therefore, no new matter is contained in the amendments and additions. Reconsideration of the present application and allowance of resulting Claims 1-52 and 87-94 is respectfully requested in view of the amendments and following remarks.

I. Rejection Under 35 U.S.C. § 103(a)

The Office Action maintained the rejection of Claims 1-8, 11-19, 21-27, 30-37, 40-45, 47-52, 87, 89-91, 93, and 94 under 35 U.S.C. § 103(a) as being unpatentable over Kresse et al. (U.S. Patent No. 6,576,221). In particular, the Office Action asserted that the claims are not limited to intracellular delivery ligands and that the prior art does not exclude intracellular delivery ligands. The Office Action also asserted that Kresse et al. disclose nanoparticles combined with a target component, and that Kresse et al. disclose that the nanoparticle compositions may contain adsorption mediatiors/enhancers and peptides. Accordingly, the Office Action asserted that a skilled practitioner in the art would recognize that the claim limitations are set forth by Kresse et al.

Applicants respectfully submit that Kresse et al. do not teach or suggest the present invention as claimed. As discussed with Examiner Jones in the telephonic interview on October 3, 2006, the present invention discloses magnetic nanoparticles for use in intracellular molecular imaging that contain both 1) at least one targeting probe, and 2) an intracellular delivery ligand. As discussed in the interview, Applicants have amended Claims 1, 9-12, 26, 28, 38, 39, 87, and 88 to clarify that the requisite "delivery ligand" is an intracellular delivery ligand. The intracellular delivery ligand facilitates the delivery of the nanoparticle across a cellular membrane or additionally across an intracellular organelle membrane. *See* page 15, paragraph [048]. The nanoparticle probes of the present invention also comprise at least one targeting probe (referred

to below as "targeting/detection probe") that facilitates the detection of a particular molecule and/or its expression levels and that may be, *e.g.*, a nucleic acid, a polypeptide, an antibody or fragment thereof, a high affinity ligand, a peptide, or an aptamer. *See* pages 18-32.

Applicants respectfully submit that Kresse et al. do not teach or suggest a nanoparticle comprising a detectable moiety with a biocompatible coating thereon and both at least one targeting/detection probe and at least one intracellular delivery ligand. Kresse et al. teach iron-containing nanoparticles having a single "targeting polymer." The nanoparticles described in Kresse et al. have two coating layers, with the outermost layer consisting of the single delivery-related component or "targeting polymer." As discussed in the interview, there is no teaching or suggestion in Kresse et al. that the addition of certain targeting/detection probes (as currently disclosed) may be used to facilitate further specificity and sensitivity of the nanoparticle probes. There is also no teaching or suggestion that specific peptides could be used for the intracellular uptake of the nanoparticles as is required by the intracellular delivery ligand component of the present nanoparticle probes. The Kresse et al. reference does suggest that the nanoparticles may comprise adsorption mediators/enhancers including peptides; however, as discussed in the interview, such peptides are included to enhance the adsorption of the targeting agent to the nanoparticle or the primary coating and not to direct the intracellular delivery of the nanoparticle. *See* Column 15, lines 24-44.

As stated previously, the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, there must be a suggestion or motivation in the reference(s) to modify the reference(s); there must be a reasonable expectation of success; and the prior art reference(s) must teach all of the claim limitations. *See* MPEP § 2143. Here, the Patent Office has not met this burden. First, the Patent Office has provided no evidence of a suggestion or motivation within the Kresse et al. reference to include both at least one targeting/detection probe and at least one intracellular delivery ligand on the nanoparticle. Second, even if one skilled in the art would have been motivated by Kresse et al. to modify the particles as disclosed in Kresse et al., there would be no expectation of success for executing this modification. Finally, the Kresse et al. reference does not teach all of the limitations of the present invention.

For at least these reasons, the Office Action failed to establish a *prima facie* case of obviousness, and Kresse et al. do not teach or suggest the presently claimed invention. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

IV. Conclusion

Applicants believe that the present application, as amended, is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The foregoing is submitted as a full and complete response to the Office Action mailed August 25, 2006.

No fees are believed due at this time. However, please charge any fees that may be due, or credit any overpayment, to Deposit Account 19-5029 (Ref.: 17625-0058). In addition, if there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited and encouraged to call the undersigned attorney at (404) 853-8000.

Respectfully submitted,

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